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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,745	04/25/2001	William C. Fanslow III	2922-A	7372

22932 7590 07/13/2004

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/842,745	FANSLOW ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 3/19/04.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-22

4a) Of the above claim(s) _____ is/are withdrawn from consideration. 5, 20-22

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 1-4, 6-19

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 3/19/04, has been entered.

Claims 1-4 and 6-19 are under consideration in the instant application.

Applicant's election with traverse of the species CD40L / soluble CD40L as the CD40 binding agent and CD30L as the additional agent as well as the election of breast cancer as the species of tumor or precancerous cell type has been acknowledged..

Claims 5, 20-22 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to a nonelected invention and/or species.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's arguments, filed 3/19/04.
The rejections of record can be found in the previous Office Action.

3. Claims 1-4, (5), 6-12 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. In evaluating the facts of the instant case, the following is noted:

It has been art-recognized experience that immunotherapy for cancer has been limited. Results obtained under controlled conditions and in inbred animals often differ from the clinical response obtained in patients. This applies in particular to strategies based on immune responses, including strategies drawn to cancer therapy. Concerning animal models, the response of animals to chemotherapy, radiation and surgery is generally predictive of their effect in human patients. Tumor burden and antigenic drift continue to present serious burdens for successful cancer therapy in vivo. Tumors are classified as immunogenic or non-immunogenic, solid or hematological in nature. Effective cancer strategies should be design to deal effectively with the nature of each of these classifications. For experimental antitumoral immunization in animals, one usually immunizes a normal animal and the effect is evaluated by the resistance to a tumor cell. For human patients, one would have to stimulate immune defense or organisms that have often carried a large tumor cell challenge.

With respect to "treating a precancerous subject" (claims 1-4, (5), 6-12), there is insufficient and guidance and direction for enabling the skilled artisan to choose those "precancerous subjects" that would be subjected to combination photodynamic and CD40L therapy. It has not been standard practice by the skilled artisan to treat precancerous subjects. The skilled artisan does not generally treat a patient with a therapeutic regimen to treat cancer prior to the diagnosis of cancer itself.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective cancer therapies for treating precancerous subjects, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed

methods to use combination photodynamic and CD40L combination therapy to treat precancerous subjects, commensurate in scope with the claimed invention.

Applicant's arguments have been fully considered but are not found convincing essentially for the reasons of record. Applicant argues in conjunction with Exhibit B (a printout of a search of a public database for English language review on human subjects published before February 2000 with precancerous in the Title) that the ordinary skilled artisan was well aware of precancerous states at the time the present application was filed.

While applicant relies upon the disclosure of Barrett's esophagus as an exemplary precancerous conditions for photodynamic therapy on page 12, lines 20-21 of the instant specification, there is insufficient direction and guidance in the specification as filed for a representative number of species to support the genus of selecting or predicting precancerous subjects and, in turn, those precancerous conditions subject to treatment with the combination of CD40 binding proteins and photodynamic therapy.

Applicant's arguments are not found persuasive.

With respect to the use of CD30L (claim 3), it is noted that specification discloses that CD30L may be administered concurrent with administering CD40 binding protein.

Applicant's arguments have been fully considered but are not found convincing essentially for the reasons of record.

Applicant submits that the skilled artisan would know how to make and use CD30L in the presently claimed invention. Applicant relies upon the instant disclosure that CD30L is a suitable agent for therapeutic use in conjunction with the invention. Applicant notes that its suitability based on its activity as a stimulus for proliferation of activated T cells as disclosed in the Goodwin et al. patent (see columns 2-3, overlapping paragraph and Examples 8 and 13 beginning on columns 30 and 34, respectively.)

However, as set forth in the prior art rejection below, Goodwin et al. teach that CD30L-conjugates can be used to treat lymphoid malignancies which express CD30 (see entire document, particularly column 11, paragraphs 3-5 to column 12, paragraphs 1-2). In addition, Goodwin et al. teach that unlabeled CD30L may be used in treating large cell anaplastic lymphoma (see column 17-18, overlapping paragraph; column 12, paragraph 4). Goodwin et al. also teach that CD30L may be used in combination with additional agents effective in treating malignancies characterized by $CD30^+$ cells (see column 17-18, overlapping paragraph).

However, the instant specification appears lacking in the teachings of how to make and use CD30L to treat tumors, broadly encompassed by the claimed methods. For example, the instant specification does not appear to distinguish the use of CD30L in the context of CD30 expressing tumor. Also, the instant specification does not appear to teach conjugating CD30L with a therapeutic agent to treat CD30 expressing tumor cells. The instant specification does not appear to distinguish treating large cell anaplastic lymphoma with unlabeled CD30L versus treating CD30 expressing tumors with CD30L conjugates.

In addition, Lynch et al. teach CD40L (page 4, columns 1-2, overlapping paragraph; page 6, column 2, paragraph 1; page 8, column 1, paragraph 1) as well as CD30 ligand antagonists (page 4, column 2, paragraph 3; page 6, column 2, paragraph 3; page 8, column 1, paragraph 1) to augment immune responses, including antitumor responses (e.g. page 7, columns 1-2). The CD30 ligand antagonists disclosed by Lynch et al. include CD30L-specific antibodies and soluble CD30 which is distinguished from the claimed methods of treating tumor bearing subjects and precancerous subjects with CD30L itself.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective cancer therapies for treating tumor bearing subjects and precancerous subjects, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods to use combination photodynamic, CD40L and CD30L combination therapy to treat cancer, commensurate in scope with the claimed invention. .

Applicant's arguments have not been found persuasive.

4. Claims 1, 2, 4 and 6-12 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Curry et al. (US 2002/0022032) AND/OR Hunt et al. (US 2003/0008857) in view of Armitage et al. (U.S. Patent No. 5,674,492) AND/OR Lynch et al. (US 2003/0165531) and further in view of Armitage et al. (U.S. Patent No. 6,410,711) for the reasons of record.

Applicant's arguments, filed 3/19/04, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant submit that the instant claims are entitled to a priority date of 4/25/00, while the provisional application associated with the prior art Curry et al. (Exhibit C) lacks any discussion of biological response modifiers such as cytokines (versus paragraph [0051] of the instant applicaton).

It is noted that the provisional USSN 60/130,519 priority document (Exhibit C) for the Curry et al. prior art clearly teaches the use of PDT in combination with immunoadjuvants (see entire document, including Summary of the Invention) as well as listing a wide variety of immunoadjuvants including cytokines (see Appendix A: Adjuvant Classification on pages 28-30, including E).

The examiner appreciates applicant's provision of the provisional USSN 60/60/130,519 priority document (Exhibit C) for review.

In addition, applicant is reminded that not all of the instant claims (e.g. claim 3) of the instant application have a priority date back to the provisional USSN 60/195,545 for the instant application. For example, the instant provisional USSN 60/195,545 does not appear to provide sufficient written description for administering the active agents recited in instant claim 3.

In contrast to applicant's assertions of the rejection is based upon an "obvious-to-try" standard; it is by now well understood that the ultimate conclusion of law that claimed subject matter as a whole would have been obvious under 35 USC 103 may at times properly be drawn from an inference of fact arising from prior art teachings which could be considered an inference that it would be "obvious to try" that which is claimed. In re O'Farrell, 853 F.2d 894, 7 USPQ 2d 1973 (Fed. Cir. 1988); Contour Saws Inc. v. Starrett Co., 444 F. 2d 433, 170 USPQ 433 (Ct.App. 1977); In re Marzocchi, 439 F. 2d 220, 169 USPQ 367 (CCPA 1977); In re Lindell, 385 F. 2d 435, 155 USPQ 521 (CCPA 1967). The evidence of purported unobvious results of record in this application is insufficient to overcome the inference of fact in this case. Therefore the above claims remain rejected under 35 USC 103 for the reasons herein and also those set forth in the previous Office Action.

In addition, applicant asserts that neither Curry et al. nor Hunt et al. teach the use of CD40L binding proteins in combination with photodynamic agents. Further, applicant asserts that neither of the Armitage et al. patents nor the Lynch et al. publications disclose nor suggest the use of photodynamic therapy.

Once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

The rejection of record is reiterated herein for applicant's convenience.

Curry et al. teach the combination of photodynamic treatment and immunoadjuvants, including cytokines (page 5, column 2 - page 7 in the treatment of tumors, including melanoma, breast cancer, colon cancer and prostate cancer (page 4, column 2, paragraph 3) (see entire document, including Description of the Related Art, Summary of the Invention, Detailed Description of the Invention and Claims).

Hunt et al. teach the combination of photodynamic treatment and apoptosis-inducing agents (see entire document, including Description of the Related Art, Summary of the Invention, Detailed Description of the Invention and Claims).

Curry et al. and Hunt et al. differ from the claimed methods by not disclosing the use of CD40L or CD30L as an adjuvant or apoptosis-inducing agent.

Armitage et al. teach methods of treating neoplastic diseases, including B lymphomas, melanoma and carcinomas that express CD40 with a CD40 binding protein, including the CD40L comprising Fc domain and leucine zippers of the instant claims (see CD40L on columns 5-10) (see entire document, including Claims). In addition to inhibiting various B cell lymphomas directly, Armitage et al. teach that it may be necessary to conjugate CD40 binding proteins with toxins or radioactive compounds (see column 12, Prevention or Treatment). In addition, Armitage et al. teach that the inventive methods may be used in conjunction with other therapies appropriate for afflicted individuals, including chemotherapy, radiation therapy and immunotherapy (see column 12, Prevention or Treatment).

Lynch et al. teach CD40L (page 4, columns 1-2, overlapping paragraph; page 6, column 2, paragraph 1; page 8, column 1, paragraph 1) as well as CD30 ligand antagonists (page 4, column 2, paragraph 3; page 6, column 2, paragraph 3; page 8, column 1, paragraph 1) to augment immune responses, including antitumor responses (e.g. page 7, columns 1-2)

Although Armitage et al. and Lynch et al. Are silent about the exact sequences of oligomeric CD40L, including oligomeric CD40-L which comprises Fc domains and leucine zippers, these references teach the same oligomeric CD40L encompassed by the claimed invention.

Although Armitage et al. ('492) teaches the CD40L employed in the claimed methods, Armitage et al. ('492) does not teach the specific sequences. Armitage et al. ('492) does teach that CD40L sequences can be found in USSN 07/969,703. Armitage et al. (U.S. Patent No. 6,410,711) is a child USSN application of USSN 07/969,703. Armitage et al. ('711) teach the sequences including those that comprise Fc domains and leucine zippers for therapeutic purposes (See entire document, including Detailed Description and Examples).

Similarly, Lynch et al. refer to PCT Publications WO 93/08207 and WO 96/40918 for sequences associated with the CD40 binding protein CD40L (see page 4, columns 1-2, overlapping paragraph). These PCT publications provide the same or nearly same teachings as Armitage et al. (U.S. Patent No. 6,410,711) with respect to the sequences associated with CD40 binding protein CD40L.

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Armitage et al. or Lynch et al to those of Curry et al. or Hunt et al. to substitute the immunostimulating properties of CD40L to a broad range of tumors as taught by Armitage et al. and Lynch et al. or the apoptotic properties of CD40L to certain types of CD40-expressing tumors as taught by Armitage et al. as the immunoadjuvant in the combination tumor therapy taught by Curry et al. or as the apoptotic agent as taught by Hunt et al.

According to Curry et al. or Hunt et al., a person of ordinary skill in the art would have been motivated to produce this resultant combination therapy with photodynamic therapy, since Curry et al. and Hunt et al. teach the advantages of combination therapy with immunostimulatory agents or apoptotic agents at the time the invention was made.

Similarly, both Armitage et al. and Lynch et al. teach combination antitumor therapy with CD40L as an immunostimulant or as an apoptotic agent. Given the properties of CD40L as an immunostimulant or apoptotic agent as taught by Curry et al. and Hunt et al., which is consistent with these properties with the teachings of Curry et al. and Hunt et al., a person of ordinary skill in the art would have recognized that the combination therapy to treat tumors with PDT and CD40L would have had a reasonable expectation of success at the time the invention was made.

It is noted that the ordinary artisan would have applied CD40L as an immunostimulant or as an apoptotic agent would have depended on the type of tumor to be treated. While the immunostimulant or adjuvant properties of CD40L would have been applied broadly against a number of tumor types, including B lymphomas, melanomas and carcinomas, the apoptotic properties of CD40L would have been limited to certain types of CD40-expressing cell types, as taught by Armitage et al.

The immunostimulant or adjuvant properties of CD40L would have been expected to stimulate various immune responses, including memory CTL to said tumor, given the teachings of both Armitage et al. and Lynch et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to substitute CD40L as the immunoadjuvant or apoptotic agents in the teachings of combined photodynamic therapy of Curry et al. or Hunt et al. In therapeutic regimens to treat tumor-bearing subjects. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

5. Claim 3 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Curry et al. (US 2002/0022032) AND/OR Hunt et al. (US 2003/0008857) in view of Armitage et al. (U.S. Patent No. 5,674,492) AND/OR Lynch et al. (US 2003/0165531) and further in view of Armitage et al. (U.S. Patent No. 6,410,711
as applied to claims 1, 2, 5 and 6-12 above and further in view of
Goodwin et al. (U.S. Patent No. 6,143,869) for the reasons of record.

Applicant's arguments, filed 3/19/04, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant asserts that the addition of Goodwin et al. does not cure the deficiencies of the first five references.

As indicated above, the teachings of Curry et al. (US 2002/0022032) AND/OR Hunt et al. (US 2003/0008857) in view of Armitage et al. (U.S. Patent No. 5,674,492) AND/OR Lynch et al. (US 2003/0165531) and further in view of Armitage et al. (U.S. Patent No. 6,410,711 provide sufficient motivation and expectation of success in providing for the ordinary artisan to substitute CD40L as the immunoadjuvant or apoptotic agents in the teachings of combined photodynamic therapy of Curry et al. or Hunt et al. In therapeutic regimens to treat tumor-bearing subjects at the time the invention was made.

The following of record is reiterated for applicant's convenience.

Goodwin et al. teach that CD30L-conjugates can be used to treat lymphoid malignancies which express CD30 (see entire document, particularly column 11, paragraphs 3-5 to column 12, paragraphs 1-2). In addition, Goodwin et al. teach that unlabeled CD30L may be used in treating large cell anaplastic lymphoma (see column 17-18, overlapping paragraph; column 12, paragraph 4). Goodwin et al. also teach that CD30L may be used in combination with additional agents effective in treating malignancies characterized by $CD30^+$ cells (see column 17-18, overlapping paragraph). Goodwin et al. also teach that CD30L can stimulate proliferation of T cells (See Analysis of Biological Activities of CD30L in Example 8 in columns 30-31 in Example 13, in columns 34-36).

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Goodwin et al. in combination with teachings of Armitage et al. or Lynch et al to those of Curry et al. or Hunt et al. to substitute the immunostimulating properties of CD40L to a broad range of tumors as taught by Armitage et al. and Lynch et al. as the additional antitumor agent as taught by Curry et al. or as the apoptotic agent as taught by Hunt et al. According to Curry et al. or Hunt et al., a person of ordinary skill in the art would have been motivated to produce this resultant combination therapy with photodynamic therapy, since Curry et al. and Hunt et al. teach the advantages of combination therapy with antitumor agents or apoptotic agents at the time the invention was made. Similarly, both Armitage et al. and Lynch et al. teach combination antitumor therapy with CD40L as an immunostimulant. Given the properties of CD40L as an immunostimulant or apoptotic agent as taught by Curry et al. and Hunt et al. and the consistency with these properties with the teachings of Curry et al. and Hunt et al., a person of ordinary skill in the art would have recognized that the combination therapy to treat tumors with PDT and CD30L as an antitumor agent (apoptotic agent or CD30L-conjugate) in combination with CD40L would have had a reasonable expectation of success at the time the invention was made. It is noted that the ordinary artisan would have applied CD40L as an immunostimulant or as an apoptotic agent would have depended on the type of tumor to be treated. The immunostimulant or adjuvant properties of CD40L would have been applied broadly against a number of tumor types, including B lymphomas, melanomas and carcinomas. The immunostimulant or adjuvant properties of CD40L would have been expected to stimulate various immune responses, including memory CTL to said tumor, given the teachings of both Armitage et al. and Lynch et al. The CD30L, including conjugates of CD30L would have been expected to treat CD30 expressing tumor cells.

One of ordinary skill in the art at the time the invention was made would have been motivated to substitute CD40L as the immunoadjuvant along with the CD30L (e.g. apoptotic agents or conjugate) in the teachings of combined photodynamic therapy of Curry et al. or Hunt et al. In therapeutic regimens to treat tumor-bearing subjects. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

6. As pionted out previously, in the interest of compact prosecution and given the election of breast cancer, the following rejection is applied even though breast cancer is not a specific limitation of the current claims.

Claims 1, 2, 4 and 6-12 stande rejected under 35 U.S.C. § 103(a) as being unpatentable over Curry et al. (US 2002/0022032) AND/OR Hunt et al. (US 2003/0008857) in view of Armitage et al. (U.S. Patent No. 5,674,492) AND/OR Lynch et al. (US 2003/0165531) and further in view of Armitage et al. (U.S. Patent No. 6,410,711 as applied to claims 1, 2,4 and 6-12 and further in view of
Hirano et al. (Blood 93: 2999-3007, 1999) for the reasons of record.

Applicant's arguments, filed 3/19/04, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant asserts that the addition of Hirano et al. does not cure the deficiencies of the first five references.

The examiner's rebuttal is set forth above.

The following is reiterated herein for applicant's convenience.

It is note that the prior art rejection above would apply to the use of CD40L as an immunostimulant in the treatment of a broad range of tumor types, including breast cancer.

Also, it was noted above that Curry et al. teach the combination of photodynamic treatment and immunoadjuvants, including cytokines (page 5, column 2 - page 7 in the treatment of tumors, including melanoma, breast cancer, colon cancer and prostate cancer (page 4, column 2, paragraph 3) (see entire document, including Description of the Related Art, Summary of the Invention, Detailed Description of the Invention and Claims).

Hirano et al. teach that CD40L can lead to decreased viability due to increased apoptosis of breast carcinoma cells (see entire document, including the Abstract, Results and Discussion). In addition, Hirano et al. teach the treatment of tumor bearing SCID mice with CD40L resulted in significant increases in survival, which would indicated that CD40L would be of clinical use to inhibit human breast carcinoma growth (see Abstract, Results and Discussion)

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Hirano et al.. in combination with teachings above that CD40L can serve as an apoptotic agent to various cancer cells, including breast carcinoma cells as well.

One of ordinary skill in the art at the time the invention was made would have been motivated to select CD40L as an apoptotic agent in the treatment of breast carcinoma in combination with photodynamic treatment as taught by Hunt et al. to treat cancer. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
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July 12, 2004